## REMARKS

Claims 32-62 were pending in the present application. This Amendment follows and makes of record a telephone interview held between Applicants' undersigned attorney, Patrick T. Skacel, and Examiner Davis, which took place on February 16, 2005. In the interview, it was brought to the Examiner's attention that the Office Action mailed December 16, 2004 failed to consider all pending claims, namely 32-62, which were presented for examination in a Preliminary Amendment filed March 11, 2002 in connection with the present application. A copy of the Preliminary Amendment as filed is attached. Applicants note, as discussed with the Examiner, that in the Preliminary Amendment, claims 56-62 were inadvertently numbered as claims 46-52, (as seen on page 4) resulting in duplicate numbering (i.e. two different claim 46's, two different claim 47's etc.). The Remarks at page 5 of the March 11, 2002 Preliminary Amendment reveal this error, referring to the pending claims as "32-62," and making it evident that Applicants intended all of the claims presented in the Preliminary Amendment (notwithstanding their incorrect numbering) to be examined. Nevertheless, it appears that the error in the claim numbering led the Examiner to consider only claims 32-55 when issuing the December 16, 2004 Office Action, which Action is in the form of a Restriction Requirement. Accordingly, as discussed with the Examiner during the telephone interview, to avoid any further confusion, Applicants are now canceling all pending claims (32-62) without prejudice and presenting a corresponding new claim set, renumbered as claims 63-93. These new claims are identical to the canceled claims except for corrections in dependencies that are more consistent

with originally filed claims 1-31 and corrections of minor typographical errors. The present Amendment does not introduce any new matter and thus, its entry is respectfully requested. Upon entry of the present Amendment, claims 63-93 will be pending and under examination.

**The December 16, 2004 Office Action**

Restriction Requirement

In the Office Action mailed December 16, 2004, the Examiner required restriction between the following groups of claims:

I. Claims 32-43, 54, drawn to a method for inhibition of apoptosis or treating diseases associated with excessive apoptosis, wherein said disease is degenerative disease.

II. Claims 32-42, 44, drawn to a method for inhibition of apoptosis or treating diseases associated with excessive apoptosis, wherein said disease is cardiomyopathy.

III. Claims 45-53, 55, drawn to a method for identifying a substance that inhibits the activity of ANT-1.

In response, consistent with the agreement reached with the Examiner during the above-noted telephone interview, Applicants are not electing a group of claims at this time. The Examiner specifically agreed that notwithstanding Applicants' absence of an election in the present response, this response will not constitute a non-responsive reply to the December 16,

2004 Office Action. Rather, in light of the confusion in the claim numbering noted above, the Examiner agreed to review and consider all claims that were previously presented in the March 11, 2002 Preliminary Amendment and now again presented as claims 63-93 in the present response, before requiring any restriction and election. Accordingly, Applicants believe that the present Amendment is fully responsive to the Office Action of December 16, 2004 and is consistent with the agreement reached with the Examiner during the February 16, 2005 telephone interview.

The Examiner is invited to telephone the Applicants' undersigned attorney if it is deemed to expedite prosecution of the present application.

Respectfully submitted,

February 16, 2004

By _____

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Attachment: Copy of Preliminary Amendment filed March 11, 2002

**PATENT APPLICATION**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

GRIMM et al.

Group Art Unit: Unknown

Application No.: New U.S. Patent Application

Examiner: Unknown

Filed: March 11, 2002

Attorney Dkt. No.: 100564-00107

For: ANT-1 AS DRUG TARGET

**PRELIMINARY AMENDMENT**

Commissioner for Patents
Washington, D.C. 20231

March 11, 2002

Sir:

Prior to initial examination of the application, please amend the above-identified application as follows:

**IN THE CLAIMS**:

Please cancel claims 1-31 without Prejudice or disclaimer.

32. A method for the inhibition of apoptosis, comprising contacting a cell with an effective amount of a substance capable of inhibiting the activity of adenine nucleotide translocase-1 (ANT-1).

33. The method of claim 32, wherein said cell is a mammalian cell.

34. The method of claim 33, wherein said cell is associated with a pathogenic disorder.

35. The method of claim 32, wherein the activity of ANT-1 is inhibited on the nucleic acid level.

36. The method of claim 35, wherein the inhibition is effected by reducing ANT-1 gene expression.

37. The method of claim 36, wherein the activity of the endogenous ANT-1 promoter is reduced.

38. The method of claim 32, wherein the activity of ANT-1 is inhibited on the protein level.

39. The method of claim 38, wherein the inhibition is effected by adding ANT-1 protein antagonists.

40. The method of claim 39, wherein the antagonist is cyclophilin D.

41. The method of claim 32, wherein an apoptosis-inducing signal transduction pathway .is inhibited, said pathway being activated by ANT-1.

42. A method for the treatment of diseases associated with excessive apoptosis, comprising the step of administering to a subject in need thereof a pharmaceutically effective amount of a substance capable of inhibiting the activity of adenine nucleotide translocase (ANT-1).

43. The method of claim 42, wherein the disease is a degenerative disease.

44. The method of claim 43, wherein the disease is dilated cardiomyopathy.

45. A method for identifying substances suitable for apoptosis inhibition comprising the step of determining the capability of a test substance to inhibit the activity of ANT-1.

46. The method of claim 45, wherein the capability of a test substance to bind ANT-1 or a domain thereof is determined.

47. The method of claim 45, wherein the capability of a test substance to bind the N-terminal domain of ANT-1 is determined.

48. The method of claim 45, wherein the capability of a test substance to inhibit the binding of ANT-1 to natural binding partners thereof is determined.

49. The method of claim 45, which is carried out as a high-throughput assay.

50. The method of claim 49, comprising a parallel determination of at least 96 test compounds.

51. The method of claim 45, which is carried out as a cell-based assay.

52. The method of claim 50, which is carried out as an assay using ANT-1-containing cell fractions or ANT-1-containing whole cells.

53. The method of claim 45, which is carried out as a molecular-based assay using an isolated protein selected from ANT-1 or a domain thereof.

54. The method of claim 43, wherein a recombinant protein is used.

55. The method of claim 45, wherein the determining step comprises the measurement of apoptosis induction.

46. The method of claim 45, wherein the apoptosis induction is measured by a parameter selected from the group consisting of DNA fragmentation, caspase activation or characteristic alterations in cell morphology.

47. A pharmaceutical composition comprising as an active agent an inhibitor of ANT-1 activity, optionally together with pharmaceutically acceptable diluents, carriers or adjuvants.

48. The pharmaceutical composition of claim 47 for use in the treatment of diseases associated with excessive apoptosis.

49. The composition of claim 48 for use in the treatment of human diseases.

50. The composition of claim 49 for use in the treatment of dilated cardiomyopathy.

51. A method for the diagnosis of an apoptotic process in a degenerative disease or a predisposition therefor comprising detecting the ANT-1 expression in a sample from tissue and/or body fluids of a subject to be tested, wherein elevated ANT-1 expression is indicative for an apoptotic process occuring in a degenerative disease or a predisposition therefor.

52. The method of claim 51, wherein the degenerative disease is dilated cardiomyopathy.

## REMARKS

Claims 32-62 are pending in this application. By this Amendment, claims 1-31 have been cancelled. No new matter is contained in the amendments.

Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300.

Respectfully submitted,

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